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| Art Unit: 1636 Phone I Mail Box and Bldg/Room Location | Number 38 <u>605 - 119</u> 7 n: <u>110 - 16</u> Res | | |
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| Please provide a detailed statement of the Include the elected species or structures, lutility of the invention. Define any terms known. Please attach a copy of the cover | keywords, synonyms, acro that may have a special m | nyms, and registry numbers, and one aning. Give examples or relevan | combine with the concept or |
| Title of Invention: | | | |
| Inventors (please provide full names): | Chiarello et | al . | |
| Earliest Priority Filing Date: | lune 28, 2001 | | |
| *For Sequence Searches Only* Please inclu appropriate serial number. | • | (parent, child, divisional, or issued p | atent numbers) along with the |
| Plane do a | chemical struct | ire search on the | linkers |
| | 1,2 and 3. | | 4 |
| Keywords; | Oligonucleotide Solid support or label or (to a | solid pliase that lakel names in Tesp. rhodomine fluor | Tableo 1, 2 and 3) |
| Attached: cop | yd Clams, | Tables 1, 2 and 3 | } |
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| Searcher Location: | Structure (#) | Questel/Orbit | |
| Date Searcher Picked Up: 811102 | Bibliographic | Dr.Link | |
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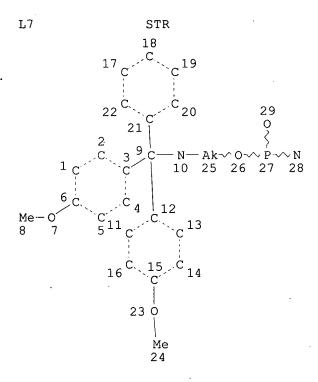
STRUCTURE FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0 DICTIONARY FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0

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NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RSPEC I NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE

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SEARCH TIME: 00.00.02

3 ANSWERS

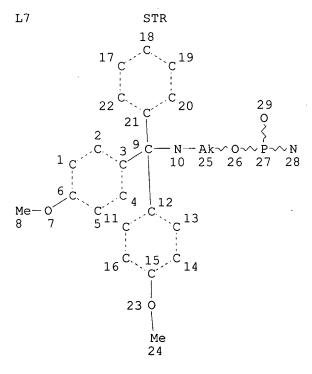
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FILE COVERS 1907 - 15 Aug 2002 VOL 137 ISS 7 FILE LAST UPDATED: 14 Aug 2002 (20020814/ED)

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NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE

L9 3 SEA FILE=REGISTRY SSS FUL L7

(L10) 66 SEA FILE=CAPLUS ABB=ON PLU=ON L9

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L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1997:155072 CAPLUS

DOCUMENT NUMBER: 126:235533

TITLE: Versatile Linker Chemistry for Synthesis of

3'-Modified DNA

AUTHOR(S): Lyttle, Matthew H.; Adams, Howard; Hudson, Derek;

Cook, Ronald M.

CORPORATE SOURCE: Biosearch Technologies Inc., San Rafael, CA, 94903,

USA

SOURCE: Bioconjugate Chemistry (1997), 8(2), 193-198

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

A general method is described for the solid phase supported synthesis of DNA contg. 3'-terminal phosphodiesters modified with linkers bearing either amino, thiol, or hydroxyl groups. These products are all made from a common intermediate, obtained by the reaction of trimellitic anhydride chloride with aminopropyl CPG. The anhydride-derivatized support was then reacted with three appropriate bifunctional spacers, giving DMT-protected hydroxyl solid supports bearing the masked functionality as an ester, amide, or thio ester. DNA synthesis was then performed, followed by ammonia cleavage and deprotection, giving the hydroxyl-, amino-, or thiol-functionalized DNA 3'-phosphate diesters, resp. Test mononucleotides synthesized with each of the new supports were identical with control mononucleotides made with 5'-immobilized nucleosides and alkyl hydroxyl, alkyl amino, and alkyl thio phosphoramidites. The new supports were then used to prep. several 3'-modified oligonucleotides, which were characterized by gel electrophoresis, HPLC, and MALDI mass spectroscopy. The amino- and thiol-functionalized DNAs were conjugated with chromophores, and purifn. of these products was facilitated by use of reversed-phase cartridges.

IT 116919-15-4

RL: RCT (Reactant); RACT (Reactant or reagent)
 (versatile linker chem. for 3'-modified DNA synthesis)

RN 116919-15-4 CAPLUS

CN Phosphoramidous acid, bis(1-methylethyl)-, 6-[[bis(4 methoxyphenyl)phenylmethyl]amino]hexyl 2-cyanoethyl ester (9CI) (CA INDEX
 NAME)

L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1994:500749 CAPLUS

DOCUMENT NUMBER: 121:100749

TITLE: Light-generated oligonucleotide arrays for rapid DNA

sequence analysis

AUTHOR(S): Pease, Ann Caviani; Solas, Dennis; Sullivan, Edward

J.; Cronin, Maureen T.; Holmes, Christopher P.; Fodor,

Stephen P. A.

CORPORATE SOURCE:

Affymetrix, Santa Clara, CA, 95051, USA Proc. Natl. Acad. Sci. U. S. A. (1994), 91(11), 5022-6 SOURCE:

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal LANGUAGE: English

In many areas of mol. biol. there is a need to rapidly ext. and analyze genetic information; however, current technologies for DNA sequence anal. are slow and labor intensive. The authors report here how modern photolithog. techniques can be used to facilitate sequence anal. by generating miniaturized arrays of densely packed oligonucleotide probes. These probe arrays, or DNA chips, can then be applied to parallel DNA hybridization anal., directly yielding sequence information. preliminary expt., a 1.28 .times. 1.28 cm array of 256 different octanucleotides was produced in 16 chem. reaction cycles, requiring 4 h to complete. The hybridization pattern of fluorescently labeled oligonucleotide targets was then detected by epifluorescence microscopy. The fluorescence signals from complementary probes were 5-35 times stronger than those with single or double base-pair hybridization mismatches, demonstrating specificity in the identification of complementary sequences. This method should prove to be a powerful tool for rapid investigations in human genetics and diagnostics, pathogen detection, and DNA mol. recognition.

TΤ 116919-15-4

RL: RCT (Reactant)

(coupling reaction of, with methyl-nitropiperonyloxycarbonyl-N-acyl deoxyribonucleoside, for octadeoxyribonucleotide combinatorial library prepn. using photolithog.)

RN 116919-15-4 CAPLUS

Phosphoramidous acid, bis(1-methylethyl)-, 6-[[bis(4-CN methoxyphenyl)phenylmethyl]amino]hexyl 2-cyanoethyl ester (9CI) NAME)

$$\begin{array}{c} \text{NH-}(\text{CH}_2)_{\,6}-\text{O-P-O-CH}_2-\text{CH}_2-\text{CN} \\ \\ \text{MeO} \\ \end{array}$$

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1994:126942 CAPLUS

120:126942 DOCUMENT NUMBER:

TITLE: Probes and method for simultaneous detection of

different DNA sequences

INVENTOR(S): Grossman, Paul David; Fung, Steven; Menchen, Steven

Michael; Woo, Sam Lee; Winn-Deen, Emily Susan

PATENT ASSIGNEE(S): Applied Biosystems, Inc., USA SOURCE:

PCT Int. Appl., 84 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

Engli

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA | TENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------|------------------|----------|-----------|-------------------------|--------------------|
| WO | 9320239 W: JP | . A1 | 19931014 | WO 1993-US3229 | 19930402 |
| | | , CH, DE | , DK, ES, | FR, GB, GR, IE, IT, LU, | MC, NL, PT, SE |
| . US | 5470705 | A | 19951128 | US 1992-866018 | 19920407 |
| EP | 635069 | A1 | 19950125 | EP 1993-912131 | 19930402 |
| EP | 635069 | B1 | 19971029 | • | |
| | R: AT, BE | , CH, DE | , DK, ES, | FR, GB, GR, IE, IT, LI, | LU, MC, NL, PT, SE |
| JP | 08504082 | Т2 | 19960507 | JP 1993-517768 | 19930402 |
| JP | 2701092 | В2 | 19980121 | | |
| PRIORIT | Y APPLN. INF | ·O.: | • | US 1992-862642 | 19920403 |
| • | | | | US 1992-866018 | 19920407 |
| | | | | US 1992-973118 | 19921106 |
| | | | | WO 1993-US3229 | 19930402 |

AB A method for simultaneous detection of .gtoreq.1 regions in a target polynucleotide is described. A plurality of different probe pairs are added to the target polynucleotide, each probe pair including 2 probes which are complementary to adjacent portions of a selected target sequence in the target polynucleotide. In each probe pair, one of the probes contains a non-polynucleotide polymer which imparts a distinctive electrophoretic mobility in a sieving matrix to the assocd. probe pair when the probe pairs are ligated. The other probe of the probe pair contains a detectable reporter label. After the probe pairs are hybridized to the target polynucleotide, the pairs hybridized to adjacent target sites are ligated. The ligated probe pairs are then released from the target polynucleotide and sepd. electrophoretically in a sieving matrix or chromatog. Two oligonucleotides designed to span the F508 region of the cystic fibrosis gene, one conjugated to an ethylene oxide polymer and the other conjugated to a fluorescent dye were prepd. This probe pair was used with a probe pair complementary to the same region of the cystic fibrosis gene on the opposite strand for ligase chain reaction detection of the cystic fibrosis mutation.

IT 116919-15-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, in prepn. of polyethylene oxide-oligonucleotide conjugate for ligase chain reaction)

RN 116919-15-4 CAPLUS

CN Phosphoramidous acid, bis(1-methylethyl)-, 6-[{bis(4-methoxyphenyl)phenylmethyl]amino]hexyl 2-cyanoethyl ester (9CI) (CA INDEX NAME)

L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1991:608442 CAPLUS

DOCUMENT NUMBER:

115:208442

TITLE:

SOURCE:

Introduction of 5'-terminal amino and thiol groups

into synthetic oligonucleotides

AUTHOR(S):

CORPORATE SOURCE:

Gaur, R. K.
Dep. Chem., Univ. Delhi, Delhi, 110 007, India
Nucleosides Nucleotides (1991), 10(4), 895-909

CODEN: NUNUD5; ISSN: 0732-8311

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S): CASREACT 115:208442

AB Oligonucleotides terminating in a 5'-primary amine group are synthesized using solid phase phosphoramidite chem. The 5'-terminal amine group in the deprotected oligonucleotide is further derivatized with N-succinimidyl-3-(2-pyridyldithio) propionate followed by treatment with dithiothreitol to produce 5'-thiol terminated oligonucleotides. Introduction of 5'-thiol group is further confirmed by reading the absorbance of the released chromophore, pyridine-2-thione at 343 nm; .epsilon.343 = 8080/M.

IT 136852-11-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, in synthesis of oligonucleotides)

RN 136852-11-4 CAPLUS

CN Phosphoramidous acid, bis(1-methylethyl)-, 5-[[bis(4-methoxyphenyl)phenylmethyl]amino]pentyl methyl ester (9CI) (CA INDEX NAME)

L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1989:8304 CAPLUS

DOCUMENT NUMBER:

110:8304

TITLE:

The preparation and application of functionalized

synthetic oligonucleotides: III. Use of

H-phosphonate derivatives of protected amino-hexanol

and mercapto-propanol or-hexanol

AUTHOR(S):

Sinha, N. D.; Cook, R. M.

CORPORATE SOURCE: SOURCE:

Chem. Div., Biosearch Inc., San Rafael, CA, 94901, USA

Nucleic Acids Res. (1988), 16(6), 2659-69

CODEN: NARHAD; ISSN: 0305-1048

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Syntheses of H-phosphonate salts RX(CH2)nOPH(0)O- QH+[I, R = 9-chloro-9-phenylxanthinyl, (4-MeOC6H4)2CPh, 4-MeOC6H4CPh2; X = 0, S; n = 6, 3; Q = (Me2CH)2NEt, 1,8-diazabicyclo[5.4.0]undec-7-ene] of N- and S-protected alcs. such as 6-aminohexan-1-ol, 3-mercaptopropan-1-ol and 6-mercaptohexan-1-ol are described using 2-chloro-5,6-benzo-1,3,2-phosphorin-4-one as the phosphonylating agent. I, in the presence of pivaloyl chloride or adamantoyl chloride as an activator, were coupled to the 5'-end of synthetic oligonucleotides on solid supports to produce amino or thio-linked oligonucleotides. Following deprotection and purifn., fluorescent dyes, biotin derivs. and poly-L-lysine-maleimide were

sep. attached to the functionalized oligonucleotides. Identical derivatized oligomers were obtained with cyanoethyl-N,N-diisopropylamidite chem. using R(CH2) nOP(OCH2CH2CN) N(CHMe2) 2 (R, n = same as above).

IT 116919-15-4P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with oligonucleotide)

RN 116919-15-4 CAPLUS

CN Phosphoramidous acid, bis(1-methylethyl)-, 6-[[bis(4methoxyphenyl)phenylmethyl]amino]hexyl 2-cyanoethyl ester (9CI) NAME)

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER:

DOCUMENT NUMBER:

1987:440272 CAPLUS

107:40272

TITLE:

Compositions and methods for functionalizing nucleic

acids

INVENTOR(S):

Snitman, David L.

PATENT ASSIGNEE(S):

AMGEN, USA

SOURCE:

PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------|--------|-----------|--------------------|----------|
| WO 8607363 W: JP | A1 | 19861218 | WO 1986-US1290 | 19860613 |
| RW: AT, BE, | CH, DE | FR, GB, | IT, LU, NL, SE | • |
| US 4762779 | A | 19880809 | US 1985-744508 | 19850613 |
| IL 79111 | A1 | 19910916 | IL 1986-79111 | 19860612 |
| EP 224578 | A1 | 19870610 | EP 1986-904012 | 19860613 |
| EP 224578 | В1 | 19900816 | • | |
| EP 224578 | B2 | 19941109 | | |
| R: AT, BE, | CH, DE | , FR, GB, | IT, LI, LU, NL, SE | |
| JP 62503099 | Т2 | 19871210 | JP 1986-503417 | 19860613 |
| JP 2534247 | B2 | 19960911 | | |
| AT 55608 | E | 19900915 | AT 1986-904012 | 19860613 |
| CA 1303526 | A1 | 19920616 | CA 1986-511560 | 19860613 |
| PRIORITY APPLN. INFO | .: | | US 1985-744508 | 19850613 |
| | | | EP 1986-904012 | 19860613 |
| | | | WO 1986-US1290 | 19860613 |
| | | | | 7 |

A method for 5'-labeling polynucleotides undergoing solid phase synthesis involves condensation of a phosphoramidite of an .omega.-hydroxyamine with a solid support-bound polynucleotide. Thus, a soln. of 0.76 mmol (Me2CH) 2NEt and 0.76 mmol [(Me2CH) 2N] PClOMe in CH2Cl2 was added to a soln. of 0.72 mmol HO(CH2)8NHDMT (DMT = dimethoxytrityl) and the mixt. was stirred at 25.degree. for 40 min to give (Me2CH) 2NPOMe[O(CH2)8NHDMT], which was coupled by the phosphoramidite method to a polynucleotide

5'-p-ACCGAATGCTCCTACAACAAGTCTC-3' bound to a solid support.

IT 109055-40-5

RL: RCT (Reactant)

(condensation of, with solid support-bound polynucleotide)

RN 109055-40-5 CAPLUS

CN Phosphoramidous acid, bis(1-methylethyl)-, 8-[[bis(4-

methoxyphenyl)phenylmethyl]amino]octyl methyl ester (9CI) (CA INDEX NAME)

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FILE COVERS 1907-1966 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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Loeb, Bronwen Friday, August 16, 2002 10:17 AM STIC-ILL

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Subject: ILL order 09/894,423

Bronwen Loeb, PhD AU 1636 703-605-1197 CM1 11D-16 Mailbox 11E-12

Appln 09/894,423

Lyttle et al (1997) Bioconjugate Chemistry 8(2): 193-198

Pease et al (1994) Proc. Natl. Acad. Sci. USA 91(11): 5022-5026

Gaur (1991) Nucleosides Nucleotides 10(4): 895-909

Sinha et al (1988) Nucleic Acids Research 16(6): 2659-2669

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